

Novel Small Molecule SIRT6 Activators/ Inhibitors



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Assigned to WARF as biological material.

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in novel compounds that could be developed into treatments for nonalcoholic fatty liver disease or cancer.

OVERVIEW

The epigenetic modifier SIRT6 is of the sirtuin class of proteins. In transgenic mice, increased SIRT6 expression lowers LDL and triglyceride levels, improves glucose tolerance and increases mitochondrial respiration. Whole-body knockout of SIRT6 leads to profound metabolic defects and an accelerated aging phenotype. Liver-specific disruption of SIRT6 increased glycolysis and triglyceride synthesis, reduced beta oxidation, and increased fatty liver formation.

Reduced SIRT6 expression is observed in human patients diagnosed with fatty liver disease, as well as those with hepatocellular carcinoma and ovarian cancer. Discovery of SIRT6 loss-of-function point mutations in human cancer patients has provided additional evidence that diminished SIRT6 function is causative for cancer. Also, sirtuin activity is linked to the inhibiting of replication of diverse viruses, such as human cytomegalovirus, influenza A (H1N1) virus and an RNA virus.

Lastly, the targeted overexpression of SIRT6 in insulin-producing beta-cells causes increased secretion of insulin in response to glucose. Thus, compounds that promote activity of SIRT6 could be useful for treating liver disease, diabetes and cancer.

THE INVENTION

UW-Madison researchers have developed three novel compounds (CL-5D, SW-055, SW-062) that activate SIRT6 in biochemical assays. Two other compounds (CL-5D-Me and SW-055-Me) are methyl esters that are not expected to be active in biochemical assays but are expected to be more cell permeable and act as prodrugs, becoming active upon ester hydrolysis in cells.

THE WARF ADVANTAGE

WARF: A Leader in Technology Transfer Since 1925

Since its founding as a private, nonprofit affiliate of the University of Wisconsin-Madison, WARF has provided patent and licensing services to UW-Madison and worked with commercial partners to transform university research into products that benefit society. WARF intellectual property managers and licensing staff members are leaders in the field of university-based technology transfer. They are familiar with the intricacies of patenting, have worked with researchers in relevant disciplines, understand industries and markets, and have negotiated innovative licensing strategies to meet the individual needs of business clients.

The University of Wisconsin and WARF – A Single Location to Accelerate Translational Development of New Drugs

UW-Madison has the integrative capabilities to complete many key components of the drug development cycle, from discovery through clinical trials. As one of the top research universities in the world, and one of the two best-funded universities for research in the country, UW-Madison offers state-of-the-art facilities unmatched by most public universities.

These include the Small Molecule Screening Facility at the UW Comprehensive Cancer Center; the Zeeh Pharmaceutical Experiment Station, which provides consulting and laboratory services for developing formulations and studying solubility, stability and more; the Waisman Clinical Biomanufacturing Facility; the Wisconsin Institute for Medical Research, which provides UW-Madison with a complete translational research facility; and the innovative, interdisciplinary Wisconsin Institutes for Discovery, home to the private, nonprofit Morgridge Institute for Research and its public twin, WID, part of the university's graduate school. The highly qualified experts at these facilities are ready to work with you to create a library of candidates for drug development.

APPLICATIONS

- Pharmaceutical development

KEY BENEFITS

- Potential drug leads

STAGE OF DEVELOPMENT

The compounds have been synthesized and tested in biochemical assays to study SIRT6 induction. Work is planned to test efficacy against viral infection. More work will need to be done to explore efficacy against other diseases.

ADDITIONAL INFORMATION

Tech Fields

Pharmaceuticals & Vitamin D - Metabolic disorders

Pharmaceuticals & Vitamin D - Oncology & hematology

Pharmaceuticals & Vitamin D - Antivirals

CONTACT INFORMATION

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847.

